

Research Article

Macroplastique and Botox are superior to Macroplastique alone in the management of neurogenic vesicoureteric reflux in spinal cord injury population with presumed healthy bladders

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Context/Objective: Vesico-ureteric reflux(VUR) is a known complication of neuropathic bladder in spinal cord injury(SCI) population. Bulking agents such as Macroplastique are new minimally-invasive treatment option for VUR with good results. The aim of this study is to assess the efficacy of Macroplastique alone or in combination with Botox(BTX-A), in managing VUR in SCI population with presumed healthy bladders and correlate the pre-and post-injection urodynamic findings with the outcome.

Design: Retrospective comparative study.

Participants: SCI patients with VUR and presumed health bladders (normo-compliant, low filling pressures), treated with macroplastique alone or in combination with BTX-A, who had pre and post-intervention Video-urodynamics (VUDS) and followed up for at least 12 months.

Interventions: Macroplastique and BTX-A injections, VUDS.

Outcome measures: The primary end point was the overall treatment rate of VUR at 3 months and the secondary outcomes were the success rate (treated + improved) and the comparison of urodynamic parameters (pre-and post-injection).

Results: We studied 34 intervention-naïve SCI patients. 19 had only Macroplastique (Group 1) and 15 had Macroplastique and BTX-A (Group 2). The overall treatment rate was 65.4% for group 1 and 88.9% for group 2 ($P = 0.029$). The overall success rate (treated + improved) was 80.8% and 94.4% respectively ($P = 0.123$). The comparison of follow up VUDS parameters showed a statistically significant rise in the detrusor pressure of group 1 (34.04cmH₂O vs.19.2cmH₂O, $P = 0.008$) and a drop in compliance (19.8mls/cmH₂O vs.26.3mls/cmH₂O, $P = 0.018$) as compared to baseline.

Conclusion: The combination of BTX-A and Macroplastique is more effective than Macroplastique alone in the management of secondary VUR in SCI patients with presumed healthy bladders.

Keywords: Neurogenic Bladder, Vesicoureteric reflux, Botulinum toxin, Macroplastique, Spinal cord injury

Introduction

A well-known complication of a spinal cord injury (SCI) is the neurogenic bladder. In suprasacral lesions, a typical neurogenic bladder is characterized by high filling pressures, poor compliance and not infrequently vesicoureteric

reflux (VUR).¹ VUR, when it presents, results in progressive upper tract deterioration and if left untreated in renal failure.² VUR is thought to be secondary to detrusor overactivity, but many studies have confirmed that VUR is not always simultaneous to involuntary detrusor contraction. Salinas *et al.*, suggested that in long standing secondary VUR, it is possible that the anti-reflux mechanism is damaged and the reflux becomes primary leading to reflux even in normal filling pressures.³

Nowdays, VUR is managed almost exclusively by sclerosing agents, administered as a single subureteric

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injection, thus minimizing the need for ureteric re-implantation which is still the golden standard and it is reserved for complicated cases.^{4,5} Matovschek in 1981, was the first to describe the endoscopic injection of Teflon for VUR correction.⁶ Since then, several bulking agents have been developed such as Polydimethylsiloxane, Polytetrafluoroethylene, Dextranomer hyaluronic acid and Glutaraldehyde Cross-linked bovine collagen etc.⁷ Numerous investigators have reported encouraging results but mainly in primary VUR.⁸ There is evidence from literature that Macroplastique (Polydimethylsiloxane: Uroplasty Inc, Geleen, the Netherlands) is effective in the management of secondary VUR due neurogenic bladder.⁹

Botulinum toxin A (BTX-A), has proved efficient in reducing intravesical pressure, improving bladder compliance and reducing incontinence episodes.¹⁰ All major organizations (NICE, EAU, AUA) recommend the use of BTX-A for refractory to anticholinergics neurogenic detrusor overactivity (Grade of Recommendation A). The two main types used are; Onabotulinum toxin A (Botox, Allergan, Irvinem USA) and the Abobotulinum toxin A (Dysport, Ipsen, Paris, France). There is evidence that botulinum toxin alone is effective in improving VUR.¹¹

A frequent dilemma in spinal multidisciplinary team meetings is the management of VUR in SCI patients with acceptable compliance and low-amplitude overactivity. The aim of this study was to compare the efficacy of the combination of Macroplastique and BTX-A versus Macroplastique alone in this population with presumed healthy bladders and correlate the pre- and post-injection urodynamic findings with the outcome.

Methods

Participants

We conducted a retrospective comparative study of spinal cord injured (SCI) patients with unilateral or bilateral vesicoureteric reflux who were managed with Macroplastique injection alone or in combination with BTX-A. We identified those with SCI related VUR with presumed healthy bladders. A presumed healthy bladder was defined as having low filling detrusor pressure (<30cmH₂O), low amplitude overactivity, good capacity (>200mls) and good compliance (>10 ml/cmH₂O). The outcomes were recorded in prospective database over a 10-year period. The inclusion criteria were: age > 18 years, no previous interventions for neurogenic overactivity, upper motor neuron lesion, baseline and follow-up videourodynamic assessment, proven VUR, adequate follow up (≥12 months) and at least 1 post-intervention annual ultrasonographic assessment of urinary tract. Patients

currently on anticholinergics were included. Patients who were known non-attenders to clinic appointments and those whose medical records were not up-to-date were excluded. All patients with VUR who were treated with ureteric re-implantation as well as those who had other treatments for overactivity (eg. sacral anterior root stimulator implant) were excluded due to difficulties in assessing postoperative outcome.

Protocol

VUR was confirmed by videourodynamics (VUDS) and graded as per the International Reflux Study Committee grading system.¹² VUDS was carried out according the Good Urodynamic Practice of International Continence Society guidelines.¹³ The examination was performed in supine position using standard urodynamic catheters (6Fr dual bladder catheter and 8Fr slit balloon rectal line) and the filling rate was set at 20 ml/min. Detrusor overactivity provocation by coughing, bending forwards and suprapubic tapping were standard maneuvers at filling phase. Voiding phase was recorded only when possible. Patients were divided into two groups; Group 1 had only Macroplastique injection while, Group 2 had Macroplastique and BTX-A injections.

The Macroplastique procedure performed in all patients under general anesthesia as a day case procedure. The details of the procedure are described elsewhere.⁸ The injection was completed when the incompetent ureteric orifice achieved a crescent-shaped appearance. Those with bilateral reflux had their treatments in two sessions starting with the ureteric unit most at risk (greater VUR grade and hydronephrotic changes). 200U of Onabotulinum toxin A (Botox) or 500U of Abobotulinum toxin A (Dysport) were administered by 15 suburothelial injections. Our trigone sparing injection protocol involved 4 injections at bladder base, 3 at each lateral wall and 5 at bladder anterior wall and dome.

All patients had a repeat VUDS at 3 months after injection and an annual US scan of the urinary tract.

Analysis

The goal of this study was to assess if the combination of Macroplastique and BTX-A is superior to Macroplastique alone in the treatment of VUR in presumed healthy neurogenic bladders. The primary end point was the overall treatment rate of VUR at 3 months between the two groups. Treatment was defined as the complete resolution of VUR in the follow up VUDS. The secondary outcomes included the success rate (treated + improved) at 3 months, the need for additional treatments and the comparison of videourodynamic parameters (pre- and post-injection).

A subgroup analysis of treated and failed cases between the two groups followed. Data was retrieved from patient records while unclear information was verified during a telephone consultation for this study purposes. The operative notes, clinical follow-ups and videourodynamic traces were reviewed.

For the statistical analysis, the statistic software SPSS (IBM® SPSS® Statistics Version 22 (IBM Corporation)) was used. The Shapiro-Wilk test used for normality before any analyses. Inferential statistics used for demographic characteristics and baseline calculations. The t-test was used for the intra-group variability and the non-parametric Mann-Whitney test to assess the variability between the two groups. The local ethics committee approved the study and patients gave their verbal consent for data publication.

Results

From 2005 to 2015, 74 SCI patients were diagnosed with VUR in our center with complete follow up data. We identified 34 intervention-naïve patients who fulfilled the inclusion criteria. 19 patients had only Macroplastique injection (Group 1) and 15 had Macroplastique and BTX-A injections (Group 2). We have studied 44 refluxing ureteric units (26 (59.1%)) in Group 1 and 18 ((40.9%) in Group 2). Before intervention 8/19 from Group 1 and 6/15 patients from Group 2 were on

regular anticholinergics. The procedures were carried out in day surgery settings. There were no postoperative complications. Basic demographics are shown in Table 1.

The overall treatment rate was 65.4% for Group 1 and 88.9% for Group 2 since 17/26 and 16/18 ureteric units respectively showed complete resolution of VUR ($P = 0.029$). The success rate (treated + improved) was 80.8% and 94.4% respectively ($P = 0.123$). A follow up ultrasonographic study at 12 months didn't show any evidence upper tract dilatation, which could be attributed to VUR. Group 1, had 4 (15.4%) ureteric units downgraded and 5 (19.2%) that failed; Group 2, had 1 ureteric unit (5.5%) downgraded and 1 failed. The patients who initially failed and 2 who downgraded underwent augmentation ileocystoplasty. 1 of them had also ureteric reimplatation. 3 of downgraded had second injection with curative intent, which was successful.

Table 2 shows the baseline and follow-up video-urodynamic findings. In Group 1, there was a significant increase in filling detrusor pressures as compared to baseline ($P = 0.008$). This was accompanied by a significant drop in compliance ($P = 0.018$), as the cystometric capacity was stable ($P = 0.147$). In Group 2, there were no statistically significant changes in the filling pressures ($P = 0.420$), compliance ($P = 0.267$) or cystometric capacity ($P = 0.614$). The intergroup differences are graphically presented in Figures 1–3. There were significant differences in filling pressures ($P = 0.038$) and bladder compliance ($P = 0.032$).

Table 3, presents the subgroup analysis of videourodynamic parameters between the two groups (treatment vs. failures) for both groups. In both groups, high post-injection detrusor pressures, small cystometric capacity, reduced compliance and higher VUR degrees characterize the failures.

Discussion

In this data analysis, we showed that the combination of Macroplastique and BTX-A injections is superior to Macroplastique alone for the treatment of secondary VUR in spinal cord injury population. To our knowledge, this is the first study that focuses specifically on presumed healthy neurogenic bladders and the first comparative study of Macroplastique and BTX-A injection versus Macroplastique alone for this population. The combination group (Group 2) had an overall treatment rate 88.9%, while Macroplastique alone (Group 1) had 65.4% ($P = 0.029$). There was no significant difference in overall success rates (94.4% vs. 80.8%, $P = 0.123$). The results were maintained at 12 months follow up, since there was no ultrasonographic evidence of upper tract dilatation.

Table 1 Basic demographic characteristics of the study groups.

	Macroplastique Group 1	Macroplastique + Botox Group 2
Sex		
Males, N(%)	13, (68.4%)	12, (80.0%)
Females, N(%)	6, (31.6%)	3, (20.0%)
Age at Injury, years, (mean, SD, range)	46.6, 18.2, (19-70)	43.3, 15.9, (15-68)
Age at Intervention, years, (mean, SD, range)	51.2, 15.6, (24-70)	48.9, 12, (24-69)
Interval from injury since VUR treatment, months (mean, SD, range)	45.5, 102, (3-384)	71.7, 113, (6-396)
Level of injury, N (%)		
C1-4	2, (10.5%)	4, (26.7%)
C5-8	2, (10.5%)	5, (33.3%)
T1-T12	12, (63.2%)	6, (40.0%)
L1-L5	3, (15.8%)	0, (0.0%)
ASIA Score, N (%)		
A	13, (68.4%)	9, (60.0%)
B	1, (5.3%)	1, (6.7%)
C	2, (10.5%)	4, (26.6%)
D	3, (15.8%)	1, (6.7%)
Unilateral VUR, N (%)	12, (63.2%)	12, (80.0%)
Bilateral VUR, N (%)	7, (36.8%)	3, (20.0%)

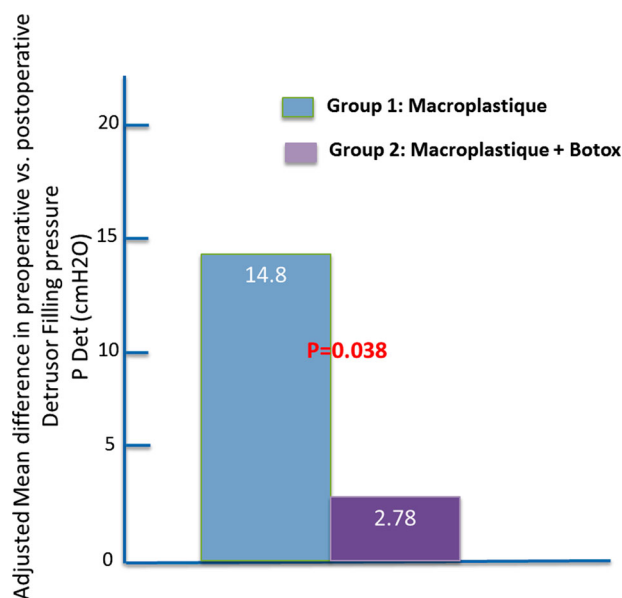
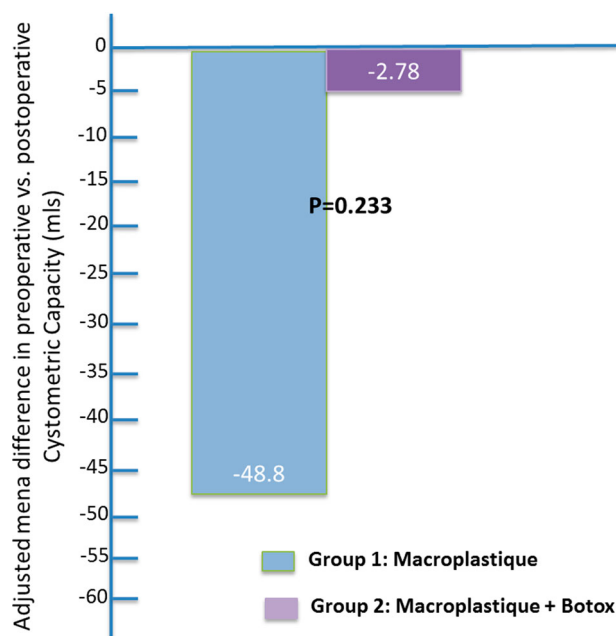
Table 2 Videourodynamic parameters, comparison between the two groups.

	Macroplastique Group 1			Macroplastique + Botox Group 2			P Value	
	Baseline	Follow up	P Value	Baseline	Follow up	P Value	Pre-treatment	Post-treatment
Filling Pdet max, cmH ₂ O (mean, SD, range)	19.2, (7.4, 10-30)	34.04, (28.1, 10-130)	0.008	21.7, (7.48, 10-30)	24.4, (16.2, 10-60)	0.420	0.315	0.259
Cystometric Capacity, mls, (mean, SD, range)	432.7, (139, 200-700)	383.8, (181.5, 100-800)	0.147	413.9, (144, 200-700)	411.1, 176.2, 100-900	0.952	0.614	0.605
VUR Grade, (mean, SD, range)	2.1, (0.59, 1-4)	na	Na	2.1, (0.6, 1-4)	na	Na	na	Na
Compliance, mls/cmH ₂ O, (mean, SD, range)	26.3, (13.9, 10-50)	19.8, (16.8, 1-50)	0.018	21.4, (11.6, 10-60)	25.61, (16.5, 1.67-50)	0.282	0.267	0.123
Detrusor								
Stable, N(%)	10 (38.5%)	7 (26.9%)		3 (16.7%)	5 (27.8%)			
Overactive, N(%)	16 (61.6%)	19 (73.1%)		15 (83.3%)	13 (72.2%)			

Although there is much data on the efficacy of bulking agents in paediatric and paediatric neurogenic population, there are only a few studies in adult patients with neurogenic bladders and especially in SCI population.^{7,14-19} Sugiyama *et al.*, reported 79% success following Teflon paste injection in 16 patients with neurogenic bladder dysfunction.²⁰ Shah *et al.*, reports 77.2% success after single or repeat injection in similar population.⁸ Polackwick *et al.*, in a series of 12 patients with neurogenic bladder showed that the success reduced to 35% at 4.5 years (58% at 12 months).¹²

It is well known that intra-detrusor BTX-A injections have a positive impact on upper tract function in patients

with neurogenic detrusor overactivity.²¹ There is sparse evidence that to a certain extent it improves VUR. Mascarenhas *et al.*, in his study on trigonal botulinum toxin injections showed complete resolution in 1 patient who had pre-injection VUR grade 2.²² Giannantoni *et al.*, in a cohort of 17 SCI patients, 3 presented with grade 3 VUR.²³ One year after 300U of Onabotulinum toxin A injection, none had persistent VUR. In addition, BTX-A intradetrusor injections, have a positive impact on recurrent urinary tract infections.¹¹ Game *et al.*, studied 30 patients with neurogenic detrusor overactivity and the found that at 6 months follow up the mean

**Figure 1** Adjusted mean difference in preoperative versus postoperative detrusor filling pressure.**Figure 2** Adjusted mean difference in preoperative versus postoperative cystometric capacity.

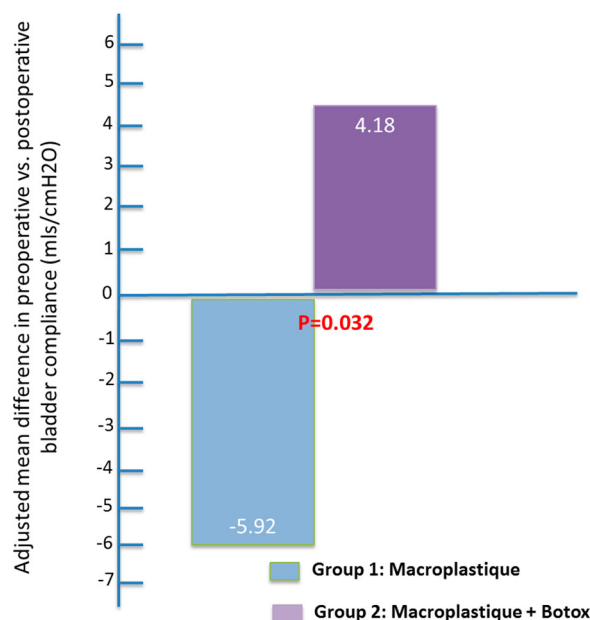


Figure 3 Adjusted mean difference in preoperative versus postoperative bladder compliance.

number of symptomatic urinary tract infections have decreased from 1.79 ± 0.39 to 0.2 ± 0.41 ($P = 0.003$).²¹ Talbot *et al.*, in 1949, conclude that kidney damage in paraplegics results from the combination of pressure related changes due to persistent hydronephrosis, and ascending urinary tract infections.²⁴ Recent evidence suggests that 750U Abobotulinum toxin A provides better outcomes than 200U Onabotulinum toxin A.²⁵ 77.8% of Group 2 had Botox and the rest Dysport. The patient that downgraded was on Botox and the one who failed on Dysport.

The efficacy of Macroplastique depends not only to the degree of reflux but to bladder status as well. A hostile neurogenic bladder (small capacity, overactive, poorly compliant) is prone to minimally invasive treatment failure. Lee *et al.*, suggested that the presence of

overactivity, high bladder filling pressures and poor compliance are risk factors for secondary VUR in the neurogenic population.²⁶ Common characteristics in our failed cases in both groups were the higher filling pressures, the smaller cystometric capacity, the higher grade of reflux and poor compliance (Table 3). We have managed these patients with augmentation cystoplasty (improves capacity, improves compliance) with excellent results. One patient had ureteric reimplantation. Zhang *et al.*, showed that augmentation enterocystoplasty without ureteral reimplantation is sufficient to treat secondary VUR in neurogenic population with treatment rate 83%.²⁷

The complication rate after Macroplastique injection is remarkably low and the results in the literature are similar. Al-Hunayan *et al.*, reported that ureteric obstruction occurred in less than 1%.²⁸ Pury *et al.*, had 1 ureteric obstruction in a series of 11 patients with neurogenic bladders.²⁹ There is evidence that Macroplastique can induce mucosal necrosis, erosion and microscopic haematuria.¹⁵ The safety of silicone is also a concern, but unlike breast implants which used silicon gels, Macroplastique is composed of solid particles.⁸ Macroplastique is a solid, elastomeric silicone which is suspended in a hydrogel carrier.⁷ Distant migration is limited by the particle size, which is greater than 100µm.³⁰ Upon implantation, the hydrogel is substituted by body fluids and host fibroblasts deposit collagen around the Macroplastique particles which hold them in place.⁸ The hydrogel is later removed by the reticuloendothelial system and excreted unmetabolised from kidneys.⁸ The most common complication after botulinum toxin injection is the urinary tract infection. Few studies report rates up to 32%.³¹ In this study there were no reported adverse events.

An interesting finding is that although the use of Macroplastique in combination with BTX-A was more

Table 3 Mean differences between treatment groups post-injection and subgroup analysis.

	Macroplastique Group 1			Macroplastique + Botox Group 2		
	Treatment	Failures	P Value	Treatment	Failures	P Value
Filling Pdet max, cmH2O (mean, SD)	3.34 (11.2)	33.34 (35.6)	<0.001	2.5 (3.5)	10 (14.1)	0.046
Cystometric Capacity, mls, (mean, SD)	-61.1 (183.3)	-68.9 (223.24)	0.664	0 (0)	-200 (212.1)	0.013
VUR Grade, (mean, SD)	2 (0.5)	2.45 (0.7)	0.035	2 (0)	3 (0)	0.017
Compliance, mls/cmH2O, (mean, SD)	-2.78 (10.8)	-6.85 (15.8)	0.726	-1.33 (1.9)	-9 (5.6)	0.23
Detrusor						
Stable, N (%)	6 (35.3)	2 (22.2)		4 (25)	1 (50%)	
Overactive, N (%)	11 (64.7%)	7 (77.8)		12 (75)	1 (50%)	

successful than Macroplastique alone, the difference between the two groups was not as much as anticipated. In an otherwise healthy bladder with grade I VUR, Macroplastique alone may be considered sufficient.

Although retrospective in nature, this study compares two commonly used treatments in this specific population group for whom there is little evidence available in the literature. We believe we have added insight into the efficacy of these treatments and the potential pitfalls in this patient group as well as advancing our knowledge of the factors that contribute to VUR development.

Conclusion

The combination of Macroplastique and BTX-A is superior to Macroplastique alone in treating the secondary VUR in presumed healthy neurogenic bladders. It is a minimally invasive procedure, quick, with a low incidence of complications and high-resolution rate. In our view, Macroplastique should be used along with BTX-A when complete resolution is desired.

Disclaimer Statements

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References

- 1 Taweel WA, Seyam R. Neurogenic bladder in spinal cord injury patients. *Res Rep Urol* 2015;7:85–99.
- 2 Cosbie RJ. Vesico-ureteric reflux in the neurogenic bladder. *Br J Urol* 1965;52:164.
- 3 Virseda MC, Salinas JC, Bolufer E, Esteban MF. Endoscopic treatment of vesicoureteral reflux with non-simultaneous involuntary detrusor contraction in chronic spinal cord injury patients with neurogenic detrusor overactivity. *Urol Int* 2014;93(4):399–402.
- 4 Lackgren G, Stenberg A. Endoscopic treatment of vesicoureteral reflux: current practice and the need for multifactorial assessment. *Ther Adv Urol* 2009;1(3):131–41.
- 5 Sung J, Skoog S. Surgical management of vesicoureteral reflux in children. *Pediatr Nephrol* 2012;27(4):551–61.
- 6 Matovscek E. Die Behandlung des vesicorenal reflux durch transurethralen einspritzung von teflonpaste. *Urologe* 1981;20:263–6.
- 7 Chertin B, Kocheron S, Chertin L, Natsheh A, Farkas A, Shenfeld O, *et al.* Endoscopic bulking materials for the treatment of vesicoureteral reflux. *Adv Urol* 2011;2011:309626. doi:10.1155/2011/309626.
- 8 Shah N, Kabir MJ, Lane T, Avenell S, Shah PJR. Vesicoureteric reflux in adults with neuropathic bladders treated with Polydimethylsiloxane (Macroplastique). *Spinal Cord* 2001;39(2):92–6.
- 9 Bartoli E, Niglio F, Gentile O, Penza R, Aceto G, Leggio S. Endoscopic treatment with polydimethylsiloxane in children with dilating vesicoureteric reflux. *BJU Int* 2006;97(4):805–8.
- 10 Weckx F, Tutolo M, De Ridder D, Van der Aa F. The role of botulinum toxin A in treating neurogenic bladder. *Transl Androl Urol* 2016;5(1):63–71.
- 11 Baron M, Grise P, Cornu JN. How botulinum toxin in neurogenic detrusor overactivity can reduce upper urinary tract damage? *World J Nephrol* 2016;5(2):195–203.
- 12 Medical versus surgical treatment of primary vesicoureteral reflux: Report of the International Reflux Study Committee. *Pediatrics* 1981;67(3):392–400.
- 13 Schafer W, Abrams P, Liao L, Mattiasson A, Pesce F, Spangberg A, *et al.* Good urodynamic practices: Uroflowmetry, filling cystometry, and pressure-flow studies. *Neurourol Urodyn* 2002;21(3):261–74.
- 14 Taskinlar H, Avlan D, Bahadir GB, Delibas S, Nayci A. The outcomes of two different bulking agents (Dextranomer hyaluronic acid copolymer and polyacrylate-polyalcohol copolymer) in the treatment of primary vesico-ureteral reflux. *Int Braz J Urol* 2016;42(3):514–20.
- 15 Bae YD, Park MG, Oh MM, Moon DG. Endoscopic subureteral injection for the treatment of vesicoureteral reflux in children: Polydimethylsiloxane (Macroplastique) versus Dextranomer/Hyaluronic acid copolymer (Deflux). *Korean J Urol* 2010;51(2):128–31.
- 16 Dodat H, Takvorian P, Mure PY, Canterino I, Poullaude JM. Analysis of the failure of endoscopic treatment of vesico-renal reflux in children using injections of Teflon and collagen and the preliminary results of injections of Macroplastique. *Prog Urol* 1995;5(1):58–68.
- 17 Warchol S, Krzemien G, Szmigielska A, Bombinski P, Brzewski M, Dudek-Warchol T. Comparison of results of endoscopic correction of vesicoureteral reflux in children using two bulking substances: Dextranomer/hyaluronic acid copolymer (Deflux) versus polyacrylate-polyalcohol copolymer (Vantrix). *J Pediatr Urol* 2016;12(4):256.e1–4.
- 18 Kocaoglu C. Endoscopic treatment of grades IV and V vesicoureteral reflux with two bulking substances: Dextranomer hyaluronic acid copolymer versus polyacrylate polyalcohol copolymer in children. *J Pediatr Surg* 2016;51(10):1711–5.
- 19 Engel JD, Palmer LS, Cheng EY, Kaplan WE. Surgical versus endoscopic correction of vesicoureteral reflux in children with neurogenic bladder dysfunction. *J Urol* 1997;157(6):2291–4.
- 20 Sugiyama T, Hashimoto K, Kiwamoto H, Ohnishi N, Esa A, Park YC, *et al.* Endoscopic correction of vesicoureteral reflux in patients with neurogenic bladder dysfunction. *Int Urol Nephrol* 1995;27(5):527–31.
- 21 Game X, Castel-Lacanal E, Bentaleb Y, Thiry-Escudie I, De Boissezon X, Malavaud B, *et al.* Botulinum toxin A detrusor injections in patients with neurogenic detrusor overactivity significantly decrease the incidence of symptomatic urinary tract infections. *Eur Urol* 2008;53(3):613–8.
- 22 Mascarenhas F, Cocuzza M, Gomes CM, Leao N. Trigonal injection of botulinum toxin-A does not cause vesicoureteral reflux in neurogenic patients. *Neurourol Urodyn* 2008;27(4):311–4.
- 23 Giannantonio A, Mearini E, Del Zingaro M, Porena M. Six year follow up of botulinum toxin A intradetrusor injections in patients with refractory neurogenic detrusor overactivity: clinical and urodynamic results. *Eur Urol* 2009;55(3):705–12.
- 24 Talbot HS, Bunts RC. Late renal changes in paraplegia: Hydronephrosis due to vesico-ureteral reflux. *J Urol* 1949;61(5):870–80.
- 25 Peyronnet B, Castel-Lacanal E, Roumiguie M, Even L, Marque P, Soulie M, *et al.* Intradetrusor injections of onabotulinum toxin A (Botox) 300IU or 200IU versus abobotulinum toxin A (Dysport) 750IU in the management of neurogenic detrusor overactivity: A case control study. *Neurourol Urodyn* 2017;36(3):734–9.
- 26 Lee JS, Koo BI, Shin MJ, Chang JH, K SY, Ko HY. Differences in urodynamic variables for vesicoureteral reflux depending on the neurogenic bladder type. *Ann Rehabil Med* 2014;38(3):347–52.
- 27 Zhang HC, Yang J, Hu HF. Augmentation enterocystoplasty without reimplantation for patients with neurogenic bladder and vesicoureteral reflux. *Kaohsiung J Med Sci* 2016;32(6):323–6.

- 28 Al-Hunayan AA, Kehinde EO, Elsalam MA, Al-Mukhtat RS. Outcome of endoscopic treatment for vesicoureteral reflux in children using polydimethylsiloxane. *J Urol* 2002;168(5):2181–3.
- 29 Puri P, Chertin B, Velayudham M, Dass L, Colhoun E. Treatment of vesicoureteral reflux by endoscopic injection of dextranomer/hyaluronic acid copolymer: preliminary results. *J Urol* 2003;170(4):1541–4.
- 30 Dodat H, Aubert Y, Chavrier Y, Geiss S, Guys JM, Lacombe A, *et al.* Vesicoureteric reflux in children: Long term results of endoscopic treatment by Macroplastique injection. *Prog Urol* 2004;14(3):380–4.
- 31 Visco A, Brubaker L, Richter H, Nygaard I, Paraiso MF, Menefee S, *et al.* Anticholinergic therapy vs. Onabotulinumtoxin A for urgency urinary incontinence. *N Eng J Med* 2012;367:1803–13.